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CARDIOVASCULAR SYPHILIS. I.

A RÉSUMÉ AND COMMENTARY

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THE subject of syphilis as it affects the heart and vessels is one which has of recent years been gradually attracting an increasing meed of attention from clinician and pathologist alike. Indeed, it bids fair to oust neurosyphilis from the prominent position occupied for so long by that condition. The present appears to be an opportune time to attempt a brief review of cardiovascular syphilis if for no other reason than the fact that at the forthcoming Annual Meeting of the British Medical Association at Manchester in July the subject has been singled out for special attention. It is to be discussed by the Section of Medicine ; and in the Section of Venereal Diseases, Professor Warthin, of the University of Michigan, is to be the reader of a paper on "The Lesions of Late Syphilis," and it is inevitable that the circulatory system will come in for a great deal of consideration.

Of all the regions of the human body there is none wherein there lurks more unsuspected syphilis than the cardiovascular system. That the vessels certainly, and the heart probably, are involved in every case of syphilis is clear when once the essential pathology of the disease is appreciated. Unfortunately, however, this appreciation is by no means general ; and it follows therefrom that much of the treatment administered is inadequate in quantity, in quality, or in both. The results of former treatment which are seen, for example in the practice of a large venereal diseases clinic, illustrate this only too well. Such a state of affairs invariably follows when therapy is based upon unsound pathology.

That syphilis is so common a cause of cardiac derangement and vascular damage is insufficiently recognised in

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general practice. Indeed, to a certain degree this also applies to hospital out-patient work, except, of course, in the special cardiological departments. Examination particularly directed to the circulatory system of syphilitic patients attending a treatment centre will show a surprising amount of cardiovascular involvement in those under treatment, and of permanent damage in those who are clinically and serologically cured. It would appear to be necessary to lay strong emphasis upon the facts that in every case of syphilis the vessels are affected from the very beginning, that the heart becomes involved at a much earlier stage than is generally realised, and that unless treatment is dictated by modern pathological knowledge, permanent damage is likely to be inflicted upon the circulatory system and a condition of *endo-syphilis* be set up.

The modern pathological view is that syphilis is essentially a disease of the blood vessels. The circulatory system is the chosen canvas upon which the *Treponema pallidum* spreads its multifarious pigments. The basic and distinctive tissue lesion of syphilis is a microscopic one. In all stages and in all organs it is in its essence identical. It begins in the perivascular lymph spaces as an infiltration of lymphocytes and plasma cells. All luetic manifestations are but varying degrees of this tissue reaction evoked by the *Treponema pallidum*, and modified according to the tissue or organ affected. All syphilis, from the alpha of the initial sclerosis to the omega of the final necrosis, has an underlying basic vascular element.

The plasma cell would appear to be the descendant of the lymphocyte and the ancestor of the fibroblast. Two types of involvement are to be distinguished in the late lesions of syphilis. Both commence in the same fashion—an early endarteritis succeeded by a periarteritis—but they differ in their end-results. In the one, the condition is an interstitial fibrosis proceeding sometimes to the formation of numerous miliary gummata. The fibrosis is replaced by scar tissue, which may eventually become calcareous. This is the type which gives rise to cirrhosis. The second type differs mainly in degree from that just described. The essential process remains the same. The final stage in this latter condition is the formation of gross naked-eye gummata with ulceration. It is important to

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note that in the case of the heart muscle the inflammation is not invariably interstitial. It may primarily involve the actual muscle fibres.

The new pathology of syphilis dates from the discovery of the *Treponema pallidum*; but it was not until the publication of Warthin's work that it was clearly set forth. To his genius, his accurate observation, and his painstaking care, medical science, and especially syphilology, owes a tremendous debt. It is greatly to be regretted that the histopathology of syphilis, with its clinical and therapeutic implications, has not yet penetrated into all the teaching schools. Much of the contemporary work published upon syphilis betrays a lack of familiarity with the modern pathology of the disease. The morbid anatomy of syphilis—and particularly of late and of endosyphilis—is still in many quarters inseparably united to the gumma. "No gummata, no syphilis" appears to be the slogan. It is essential in these days, when assessing the value of any work relative to syphilis, that the first consideration to be taken into account is the pathological criteria upon which the investigation is based. Unless this is modern in character and built upon the foundations laid down by Warthin, anything erected thereon is practically valueless. While giving full honour to the Old Masters of Pathology, it is idle to deny that the conception of syphilis as envisaged by Morgagni, Virchow, Rokitanski, Wagner, and Baümle is obsolete and misleading. Unfortunately, it has not yet been erased from all the text-books, and, in consequence, much clinical and therapeutic work continues upon wrong lines. There are still clinicians—and perhaps pathologists too—whose camp is still pitched under the shadow of the gumma. The fact is that the overwhelming proportion of luetic infections run their course without gummatous formation. The type-lesion of the disease—first, last, and all the time—is that of a mild inflammatory process characterised by an infiltration of lymphocytes and plasma cells, particularly in the stroma around the blood vessels and lymphatics. Slight tissue proliferations subsequently occur, and these proceed eventually to fibrosis, with atrophy and degeneration of the parenchyma.

Contrary to what appears to be the general conception, the majority of syphilitics who die from their disease succumb not to locomotor ataxia or paresis, but to

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cardiovascular syphilis, especially in the form of chronic myocarditis. The best index of the progress or regress of syphilis in the country is afforded not by the mortality figures for tabes and general paralysis, but by those from cardiovascular disease as worked out by Osler. Only rarely do sufferers from syphilis die from central nervous system involvement.

Probably from the very earliest clinical evidences of syphilis—certainly from the commencement of the so-called “secondary” period—onwards, microscopic lesions are found in the heart and great vessels characteristic of treponemal localisation and activity. These vary greatly in degree of severity. In most cases, cardiac and vessel fibrosis can only be demonstrated by the microscope. It is most likely to be found in the anterior wall of the left ventricle near the apex, the adjacent portion of the septum, and the posterior wall of the left ventricle near the attachment of the mitral valve. Naked-eye evidence of fibrosis may be present ; but its absence is no criterion of the non-existence of syphilis. In most of the post-mortem studies done in this country, the presence or absence of the disease is decided by gross rather than by microscopic evidence. Such antiquarianism means that only an infinitesimal amount of post-mortem syphilis is uncovered, and this must react profoundly upon clinical work. The ubiquity of the disease is not appreciated ; its clinical recognition is obscured ; unduly optimistic prognoses are made ; therapy lacks thoroughness ; and it is not realised that even after the most prolonged treatment, the cardiovascular system of the average syphilitic who is clinically and serologically cured is permanently “damaged goods.” His grip upon life is appreciably weakened.

In the early stage of generalised syphilis very evident disturbances of the cardiac rate and rhythm are common. In something like 50 per cent. of cases a definite bruit is to be made out. Brooks performed 50 consecutive post-mortems upon persons with cardiovascular syphilis and found that in 28 cases the pericardium was involved, in 44 the myocardium, gummata of the heart were found on 5 occasions, while the coronary arteries were affected in 35 instances. Warthin's experience is that in 85 per cent. of syphilitics who arrive at the post-mortem room, the heart is diseased.

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Cardiovascular syphilis may conveniently be classified in the following manner :—

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| I. Pericarditis and epicarditis. | } | (1) Diffuse.
(2) Localised (gumma). |
| II. Myocarditis . . . | { | (1) Parenchymatous.
(2) Interstitial.
(3) Diffuse.
(4) Involving bundle of His. |
| III. Endocarditis . . . | . | Aortic insufficiency. |
| IV. Coronary arteritis. | | |
| V. Aortitis . . . | { | (1) Without dilatation.
(2) Fusiform dilatation.
(3) Aneurism. |
| VI. Peripheral arteritis . | { | (1) General arteriosclerosis (with or without hypertension).
(2) Local arteriosclerosis.
(3) Aneurisms. |
| VII. Peripheral phlebitis . | { | (1) General.
(2) Local with thrombosis. |
| VIII. Vasomotor disturbance | | Raynaud's disease (?). |

Pericarditis and Epicarditis.—Syphilitic pericarditis is apparently a much more common condition than clinical experience would suggest. Brooks found it in 50 per cent. of luetic hearts. He described pericardial patches which he likened to leucoplakia. An inflammation of the pericardium, usually too slight to secure clinical recognition, is not infrequently found in association with aortitis and aortic aneurism. The occurrence of adhesions or definite pericardial thickening on the anterior aspect of the heart just above the apex is strongly suggestive of syphilis. Histological examination of the patch and of the subjacent myocardium will either confirm or deny the suspicion.

When so severe as to give rise to clinical signs, syphilitic pericarditis presents of itself no specific diagnostic picture. The manifestations are those of an ordinary pericarditis; and it is only by a careful examination of the case from every angle that the syphilitic ætiology may be laid bare. Heimann, Strachan, and Hayman in a preliminary note

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on cardiac disease among South African non-Europeans mention that syphilitic pericarditis, while sometimes seen, is rare. It appears as an effusion accompanied by failure of compensation, the clinical signs being those of pericardial effusion. Vigorous antisymphilitic therapy is stated to be sometimes successful. Donnison, in a reference to Heimann's paper, mentions that he has reported a case of syphilitic pericarditis which appeared to be a "gummatous pericarditis and myocarditis." In examining syphilitic patients I have occasionally heard at the apex fine crepitations systolic in time. These are often intensified by pressure, and I am inclined to consider them at least suggestive of syphilitic pericarditis. As is mentioned by Osler and Gibson, an unusual form of pericardial involvement is that in which the smaller pericardial arterioles are dotted with numerous small aneurisms accompanied by much thickening of, and adherence between, the pericardium and epicardium. Syphilis of the mediastinum and pulmonary syphilis, especially at the root of the lung, may induce a pericarditis.

Myocarditis.—In the parenchymatous variety, large colonies of treponemata may be found when the tissue is stained by the Levaditi method. These colonies are chiefly seen in the tissue spaces and around the blood vessels. They may give rise to no tissue reaction. Pale degeneration of the heart muscle may be seen which is of the nature of a liquefaction necrosis. Fatty degeneration may be the predominating or the sole condition associated with colonies of *Treponema pallidum*. Such areas are focal and may be seen with the naked eye as small yellowish spots. At times these are found to have become calcified. The specific change in the heart muscle may simply consist of atrophy of the muscle fibres. In all these conditions Warthin was able to demonstrate the presence of treponemata. The pale degeneration of the muscle substance is to be identified by the fact that the tissue fails to stain with eosin, and that the muscular striations tend to disappear. Where the process is advanced, it may be impossible to tell where muscle ends and connective tissue begins. In virulent congenital cases, necrosis is present. The condition is quite independent from, or secondary to, any vascular condition. It is primary in character and is due entirely to the local

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reaction set up by the presence of large numbers of treponemata.

The interstitial type of proliferation is always perivascular in origin, and it presents the characteristic histological picture. Œdematous areas are present, especially in congenital cases, and so likewise are patches of myxomatous degeneration. Both these are found to be thronged with treponemata. The interstitial infiltrated areas are but rarely focal or circumscribed. This serves in some measure to distinguish a treponemal from a streptococcal myocarditis.

The whole thickness of the myocardium, not excluding the papillary muscles, may be affected. As a rule, however, the inflammatory area lies nearer to the endocardium, and it tends to spread more readily in that direction than deeper into the muscle. In congenital cases, on the other hand, it is more common for the myocarditis to begin nearer the epicardium and to progress still further in that direction. In acquired syphilis, then, the usual course is for a myocarditis to progress towards an endocarditis, while in congenital syphilis the consequence of myocarditis is more commonly a pericarditis. Some of the primary or so-called "idiopathic" cases of pericarditis seen in children are manifestations of congenital syphilis. It is important to keep congenital syphilis in mind as an ætiological factor in Pick's disease—pericardial pseudocirrhosis. In this condition, in addition to peritonitis, ascites, perihepatitis, and cirrhosis, there is often in early life an adherent pericardium associated with chronic mediastinitis with adhesion between the epicardium and the pleura and chest wall. The result is great cardiac hypertrophy and dilatation.

Luetic myocarditis has been known to occur immediately after the appearance of the chancre and before any general cutaneous eruption. Recent observation and experience seems to indicate that except in the very early primary cases, myocarditis always occurs in some degree. It is the forerunner of pericarditis, endocarditis, valvular damage, coronary arteritis, and aortitis in most, if not in all instances. To exaggerate its importance is almost impossible; and the prudent attitude for the clinician to adopt is to regard every syphilitic with whom he is called upon to deal as suffering from syphilis of the myocardium. Treatment must be of such a character, be

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instituted at so early a date, and be pursued for so long a period that permanent damage to the heart muscle may be avoided or minimised. Absolute certainty of forestalling myocardial fibrosis can only be assured by the prompt, vigorous, and prolonged treatment of syphilis immediately upon the appearance of the initial sore and before the serological test gives a positive result.

When a patch of fibrosis reaches the surface of the myocardium, the overlying epicardium or endocardium becomes thickened and roughened. Adhesions form, and their common site is just above the apex on the anterior wall of the left ventricle. It is in this region that aneurism and rupture of the heart may occur.

In advanced cases of syphilitic myocarditis, the condition is most marked around the smaller coronary arterioles. Syphilis appears to have a special affinity for these vessels, and they may show involvement even before the appearance of the cutaneous eruption. Although it is probably true that in the majority of cases the myocarditis, fibrosis, and necrosis is secondary to coronary endarteritis, yet it has been conclusively shown that syphilitic myocarditis may be a primary condition.

In its earliest stages syphilitic myocarditis is asymptomatic, but it is important that the thought of such an entity should enter the clinician's mind at the earliest possible moment. Syphilis is a terribly un-original disease. It is, as Hutchinson said, "The Great Imitator." Its main characteristic is that it can produce in any human tissue or organ, lesions which are more frequently the products of other diseases. Syphilis should always be eliminated before a diagnosis is made and therapy commenced. The routine serological test is long overdue.

The certain signs of syphilitic myocarditis have yet to be discovered, and at the present moment the clinician must grope his way through a jungle of indefinite twilight. In the past, perhaps, a little too much attention was concentrated upon the valves of the heart, and diagnosis was chiefly taught by the differentiation of murmurs. Although it was emphasised by the earlier cardiologists that the heart muscle was all-important and that the prognosis of any cardiac affection depended upon the state of the myocardium, yet that fact receded into the clinical background. It is only within comparatively

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recent years that the myocardium has received the attention it deserves. Death is held off by the valour of the myocardium. Myocarditis is a cur that bites without preliminary growling, whereas the loud bark of the valvular bruit is very often edentulous.

A certain degree of myocarditis is present in all patients who progress beyond the early initial stages of syphilis. It may actually manifest itself contemporaneously with the initial sclerosis. Hazen records a case occurring in a physician where a serious myocarditis developed before the appearance of the rash. Tachycardia, arrhythmia, and intermittence are pointers for which to watch in the early syphilitic. These by themselves are, of course, of no real diagnostic value so far as syphilis is concerned, with respect to persons presenting no other signs of that disease. Nevertheless, experience in their observation and in their disappearance under treatment has brought conviction that they are of importance in the early stages of the disease as indicating that the attack upon the heart has commenced.

During the post-primary period of the disease, extrasystoles may be present. In early cases, these are sometimes found to occur during the first week or two of treatment, which is somewhat suggestive that they may be of the nature of a Herxheimer reaction. Hypertension is also sometimes developed under treatment in young subjects. Cardiac pain—or it may be merely a “heart sense”—is common. Harris found that pain was the presenting symptom in 70 per cent. of hisluetict heart cases.

The electrocardiograph must surely prove of great value ; and it is probable that those who have the opportunity for making extensive use of it may discover some pointers suggestive of, or perhaps even diagnostic of, syphilitic myocarditis. My personal experience of such work is so slight as to prevent me from speaking, but Harris gives it as his opinion that there is a type of electrocardiogram which is characteristic. He omits to give an illustration, but states that it consists of certain wavelets all over the electric line. There is some valuable work waiting to be done by collaboration between the venereal diseases treatment centre and the cardiological department of a hospital. At the present time, however, all that the electrocardiogram yields is a

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general statement as to the condition of the heart muscle without any indication as to cause.

In auscultating the hearts of syphilitic patients there is sometimes heard, especially in cases of several years' standing, a somewhat musical apical systolic bruit indicating mitral incompetence. This I believe to be due, not to any damage to the valve segments, but to a fibrosis of the myocardium at the valve attachment causing a lack of coaptation of the segments with incomplete closure.

Saggiaro investigated the cardiac condition of twenty patients suffering from secondary syphilis. These were all young men in whom circulatory disturbance due to age or alcohol could be ruled out. The conclusions arrived at were: (1) that patches of myocarditis are the rule in secondary syphilis; (2) that the usual symptoms are tachycardia and dyspnoea; (3) that clinical examination shows an enfeebled myocardium with frequently an increase in the transverse diameter of the heart, irregular and small pulse, and blurred heart sounds; (4) that myocardial fibrosis may involve the terminal branches of the vagus nerve leading to disturbances of innervation which manifest themselves as extra-systoles, tachycardia, palpitation and an exaggeration of the oculo-cardiac reflex. The cardiac function should always be investigated by the application of Katzenstein's test and the oculo-cardiac reflex. In the former, myocardial efficiency is indicated by an increase of blood pressure during constriction of the femoral artery. The latter reflex is elicited by firm compression of both eyeballs backwards into the orbits. Normally, this causes an immediate slowing of the heart rate by six to eight beats per minute, accompanied, it may be, by extra-systoles. The slowing ceases immediately the pressure is removed.

Heart-block.—In dealing with this matter it is important to keep in mind that heart-block and the Stokes-Adams syndrome are not different names for the same thing. The former may occur without the syndrome, and it in turn may be due to causes other than disease of the auriculo-ventricular bundle. Heart-block is commonly, but the Stokes-Adams syndrome only occasionally, due to syphilis. Heart-block is brought about by arteriosclerosis of the vessels supplying the bundle, by fibrosis or gumma of the bundle itself, or by pressure from

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adjacent fibrosis or gumma external to the bundle. Where the condition is due to arteriosclerosis, little or nothing is to be hoped for from treatment. When the other conditions are operative, however, treatment is most effective.

In mapping out treatment it is essential to keep in mind that the bundle of His is very susceptible to any toxic agent ; and in those cases where heart-block is due to some cause other than syphilis, the administration of an arseno-benzol compound may have a seriously damaging effect upon the structure itself. Indeed, as has been pointed out by Bickel, arsenobenzenes acting upon a myocardium damaged by syphilis or any other cause may set up a grave derangement of the conducting function of the bundle. It may actually produce a condition of heart-block where none previously existed. Bismuth or the pentavalent arsenicals are practically free from this danger.

(To be continued)

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